REMARKS

Reconsideration and allowance of the present application based on the following remarks are respectfully requested.

Upon entry of the above amendments, claims 8-15 and new claims 35-36 will be before the Examiner for reconsideration while claims 1-7 and 16-34 remain as withdrawn claims, pursuant to a requirement for restriction.

As suggested, "Gram +ve" is changed in all claims where it appears to "Gram positive." Also, the actual structural formula from Figure 2, is bodily incorporated into claim 8, and identified, for simplicity in subsequent references in dependent claims, as "Formula (I)." The multiple dependencies in claims 11-15 have been amended to refer to only the non-multiply dependent claims 8 and 9. New claim 35 corresponds to previous claim 15/8 or 9/7/5. Also, all parenthetical expressions have been deleted or taken out of parentheses with appropriate modifications as necessary to maintain the same meanings as in the original claims. In this regard, new claim 36 is directed to the testing for infection in humans.

Accordingly, no new matter is added by any of the claim amendments.

The objection to claim 12 is respectfully traversed.

Whereas main claim 8 is directed to a method for testing for Gram positive bacterial infection, claim 12 is directed to a method for detecting infection caused by Gram positive cocci. Therefore, claim 12 does further limit claim 8 which includes, for example, detecting for infection caused by Gram positive bacilli (i.e., rod shaped), which as those skilled in the art are aware, are also capable of causing infection.

The replacement of "Gram positive" for "Gram +ve" overcomes the rejection under 35 USC 112, second paragraph.

With regard to the suggestion that the application was filed without drawings, such suggestion is not understood and is considered to be incorrect.

The subject application was filed as the Section 371 National Phase entry of PCT/GB99/01650, which includes 8 sheets of drawing figures, forming part of the subject application. For the Examiner's convenience a copy of the original drawing figures (Substitute Sheets, Rule 26) are enclosed.

Accordingly, the introduction of the structural formula from Figure 2, is not new matter.

Claims 8-13 and 15 are rejected under 35 USC 102(b) as anticipated by Carruthers et al (J. of Clinical Microbiology, April 1984, p. 552-554).

As described in the application, and as shown in Figure 2, now explicitly incorporated into claim 8, the subject matter under consideration involves the use of a novel form of lipoteichoic acid (LTA), namely, wherein, as noted by the value of "n" in Formula (I) is from 3 to 10, inclusive, is of relatively short chain length.

In contrast, as noted on page 552, right column, 4th full paragraph, the LTA obtained by and described in Carruthers was derived from the whole cells (pellets extracted with phenol), and processed by the techniques described in the paper by Fischer et al (J. Biol. Chem, 255, 1980:4557-4562)(copy enclosed).

As described by Fisher et al, the chain length of the *Staph. aureus* LTA, determined from the glucose:phosphorus ratio, was between 18 and 22 glycerol phosphate units (see Results, Table III, p. 4560, and, particularly, column a of "Mean Chain Length"). This would correspond to a value of "n" in the formula (I) of from 18 to 22, whereas, as set forth in the claims, the value of "n" is, at a maximum, 10, or less.

Therefore, since Carruthers used the same TLA as in Fischer and further, since there is simply no disclosure or suggestion of using or preparing TLA with chain lengths shorter than 18 glycerol phosphate units, the disclosure of Carruthers does not anticipate the subject matters of claims 8-13 and 15.

Claims 8-13 and 15 are also rejected under 35 USC 102(b) as anticipated by Wergeland et al (J. of Clin. Microbiology, June 1989, p. 1286-1291).

This rejection is respectfully traversed for the following reasons.

As was the case with Carruthers, the LTA used as antigens in the studies reported by Wergeland, necessarily, because it was extracted from cells using phenol, in the same manner as described by Fischer et al, has a glyerolphosphate chain length of 18 or more units, in contrast to the 10 or fewer units in the LTA used in the present invention.

Thus, as described under "MATERIALS AND METHODS" page 1286, right column, LTA was purified from *S. aureus* as described by Aasjord et al, Acta Pathol. Microbiol. Scand. Sect. C 88:439-448 (1980), which in turn, uses methodology devised by Moskowitz [J. Bact., 91:2200-2204 (1966), copy enclosed] and Ofek et al [J. Exp. Med. 141:990-1003 (1975), copy enclosed] (see, e.g., page 132, lower left column under "*Isolation of LTA*").

However, since the initial extraction is from cells, with phenol, regardless of the purification technique, the LTA is considered to fall within the ranges shown by Fischer, namely, wherein "n" ranges from 18 to 22.

As such, the disclosure by Wergeland fails to anticipate any of the subject matters of claims 8-13 and 15

Claims 8 and 14 are rejected under 35 USC 103(a) as unpatentably obvious over Wergeland et al in view of Raad, (The Lancet, March 21, 1998).

This rejection is respectfully traversed for the following reasons.

As discussed above, Wergeland et al do not suggest using the instant LTA, having the structure of Figure 2 and Formula (I), as antigen, or for any other purpose, in a test for infection by Gram positive bacteria.

Therefore, since Raad does not supply this deficiency, the inventions defined in Claims 8 and 14 would not have been prima facie obvious.

Incidentally, for further understanding, the Applicants are also submitting herewith a copy of a recent paper published by the present inventors and their colleagues, Lambert et al, FEMS Immunology and Medical Microbiology 29: 195-202 (2000). In this paper the authors explain that the short chain lipoteichoic acid, forming the basis of the present application and claims, was obtained from the extra-cellular medium of bacterial cultures, (see, also the present specification, e.g., paragraph bridging pages 11-12). As pointed out above, this is in direct contrast to the source of LTA in the cited literature, namely, by phenol extraction from bacterial cells (cell walls and membranes).

The enclosed article explains that mass spectometry experiments showed that "in contrast to the culture supernatants, the phenol-extracted LTA from *Staphylococcus epidermidis* NCIMB 40896 did not give the M/Z peaks at 804 and 1206. Instead, the mass spectrum contained a single major peak at 450 together with other minor peaks which were deconvoluted to give a total mass of 18474.59 and a total negative charge (i.e., chain length) of 40-42" (see page 199, left hand column).

Again, it is evident that the cited prior art represented by Carruthers and Wergeland, do not disclose or suggest the instant short chain LTA having the structure of formula (I).

Regarding the mentioned publications by Elliott (1997) and by Oltvoort (1982), it is first noted that the Elliott paper was published in 1999, not 1997, and is not prior art to the present application and, moreover, represents work reported by one of the present inventors. Applicants also agree that Oltvoort should not be cited in a rejection of the present claims noting, in particular, that this paper merely describes a synthesis route for a membrane teichoic acid fragment of *Staphylococcus aureus* and does not suggest any use for the so prepared fragments. Moreover, as shown in Fig. 1 of Oltvoort, the membrane teichoic acid has 15 glycerolphosphate units. There is no suggestion to prepare or utility of shorter chain length molecules.

In view of the foregoing, the claims are now believed to be in form for allowance, and such action is hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned at the telephone number listed below.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached Appendix is captioned **"Version with markings to show changes made"**.

All objections and rejections having been addressed, it is respectfully submitted that the present application is in a condition for allowance and a Notice to that effect is earnestly solicited.

Respectfully submitted,

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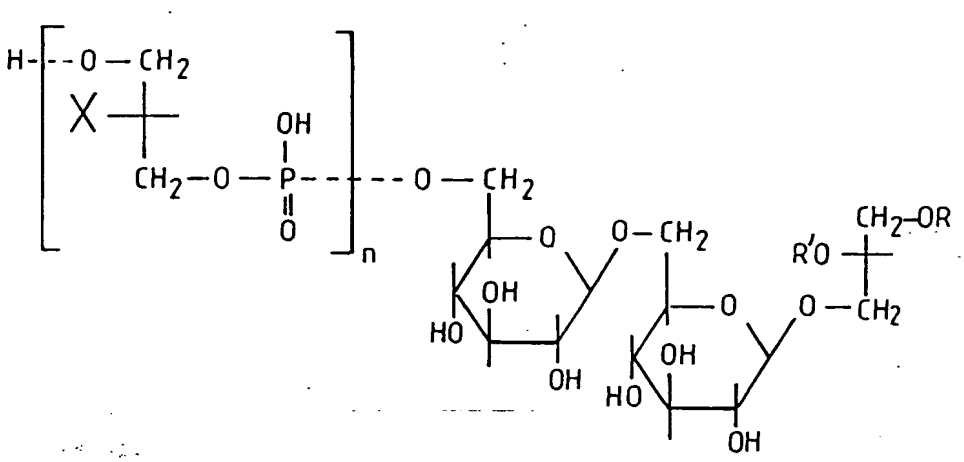
Drawing Figures (8 sheets)

APPENDIX: VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

8. (Amended) A method of testing for Gram [+ve] positive bacterial infection in a mammalian [(typically, human)] subject, the method comprising the steps of: obtaining a sample of body fluid from the subject; contacting the sample with a composition comprising a compound having the structure [shown in Figure 2] of the following formula (I),



wherein,

n is an integer between 3 and 10, [(] inclusive,[)] and

X is H, OH, alkyl, aryl, amyl, or an amino acid residue, which may be [(optionally] substituted[)] or a sugar residue, which may be [(optionally] substituted[)], and

R and R^1 may be the same or different, and are hydrophobic hydrocarbon or fatty acid chains[(R may be the same as R^1, or different)]; and

Detecting binding of antibodies, [(] if any[)], in the sample to the composition.

11. (Amended) A method according to any one of claims 8, or 9 [or 10], wherein the test method comprises the performance of an enzyme-linked immunosorbent assay [(ELISA)], radioimmunoassay [(RIA)], or a Western blot.

12. (Amended) A method according to any one of claims 8 [to 11] or 9, for testing for infection caused by Gram [+ve] positive cocci.

13. (Amended) A method according to any one of claims 8 [to 12] or 9, for testing for infection by a Streptococcus, a Staphylococcus, or an Enterococcus.

14. (Amended) A method according to any one of claims 8 [to 13] or 9, for diagnosing the presence of a Gram [+ve] positive infection associated with a central venous catheter, a cerebrospinal fluid shunt or a prosthetic device.

15. (Amended) A method according to any one of claims 8 [to 14] or 9, wherein the composition [is in accordance with any one of claims 5-7] comprises a compound of formula (I) in substantially pure form, wherein

n is an integer between 3 and 10, inclusive, and

X is H, OH, alkyl, aryl, amyl, or an amino acid residue, which may be substituted, or a sugar residue, which may be substituted, and

R and R^1 may be the same or different, and are hydrophobic hydrocarbon or fatty acid chains.